

CLAIMS:

1. A method for determining the presence or absence of a cancer in a patient, the method comprising the steps of:
 - 5 (a) determining the level of Pygopus gene expression in a biological sample obtained from a patient, and
 - (b) comparing the level of Pygopus gene expression in the biological sample to a predetermined cut-off value, to determine whether Pygopus expression is higher in the
 - 10 biological sample;therefrom determining the presence or absence of cancer in the patient.
2. A method for monitoring the progression of a cancer in a patient, the method comprising the steps of:
 - 15 (a) determining the level of Pygopus gene expression in a biological sample obtained from a patient, and
 - (b) comparing the level of Pygopus gene expression in the biological sample to a predetermined cut-off value, to determine whether Pygopus expression is higher in the
 - 20 biological sample; and therefrom determining the presence or absence of cancer in the patient;
 - (c) repeating steps (a) and (b) using a biological sample obtained from the patient at a subsequent time; and
 - (d) comparing the level of Pygopus gene expression
 - 25 detected in step (c) to the level of Pygopus gene expression detected in step (b); and therefrom monitoring the progression of the cancer in the patient.

3. The method according to claim 1 or 2 wherein the predetermined cut-off value is the level of Pygopus gene expression in a normal biological sample.

4. The method according to any one of claims 1 to 3
5 wherein the cancer is ovarian cancer, and the biological sample is a tissue biopsy containing epithelial ovarian cells.

5. The method according to any one of claims 1 to 3
10 wherein the cancer is breast cancer, and the biological sample is a tissue biopsy containing mammary cells.

6. The method according to any one of claims 1 to 5 wherein the Pygopus gene is hPygo2 as shown in SEQ ID NO:1.

7. The method according to any one of claims 1 to 5 wherein the Pygopus gene is hPygo1 as shown in SEQ ID NO:3.

15 8. The method according to any one of claims 1 to 7 wherein the level of Pygopus gene expression is determined by the amount of Pygopus protein.

9. The method according to any one of claims 1 to 7
20 wherein the level of Pygopus gene expression is determined by the amount of Pygopus mRNA.

10. A kit for determining the presence or absence of a cancer in a patient, the kit comprising a reagent capable of detecting Pygopus protein or mRNA in a biological sample obtained from the patient, and instructions for using the
25 reagent to determine whether the level of Pygopus gene expression in the biological sample is higher compared to a predetermined cut-off value, and therefrom determining the presence or absence of cancer in the patient.

11. The kit according to claim 10 wherein the reagent is an antibody specifically reactive to Pygopus protein.

12. The kit according to claim 10 wherein the reagent is a polynucleotide capable of binding to a Pygopus gene or
5 to a part of a Pygopus gene.

13. The kit according to any one of claims 10 to 12 wherein the predetermined cut-off value is the level of Pygopus gene expression in a normal biological sample.

14. The kit according to any one of claims 10 to 13
10 wherein the cancer is ovarian cancer, and the biological sample is a tissue biopsy containing epithelial ovarian cells.

15. The kit according to any one of claims 10 to 13 wherein the cancer is breast cancer, and the biological
15 sample is a tissue biopsy containing mammary cells.

16. The kit according to any one of claims 10 to 15 wherein the Pygopus gene is hPygo2 as shown in SEQ ID NO:1.

17. The kit according to any one of claims 10 to 15 wherein the Pygopus gene is hPygo1 as shown in SEQ ID NO:3.

20 18. A human Pygopus polypeptide which lacks the plant homeodomain (PHD) sequence and the N-terminal homology domain (NHD) sequence.

19. The polypeptide according to claim 18 which is hPygo-2 (SEQ ID NO:2) lacking amino acids 89-328.

25 20. The polypeptide according to claim 18 which is hPygo-1 (SEQ ID NO:4) lacking amino acids 85-341.

21. A nucleic acid encoding the polypeptide according to any one of claims 18 to 20.
22. The nucleic acid according to claim 21, comprising nucleotides 437-1156 of SEQ ID NO:1.
- 5 23. The nucleic acid according to claim 21, comprising nucleotides 253-1023 of SEQ ID NO:3.
24. An antibody specifically reactive with the polypeptide according to any one of claims 18 to 20.
25. The antibody according to claim 24 which is a
10 monoclonal antibody.
26. A method for obtaining a compound which inhibits tumor cell proliferation, wherein the tumor cell expresses Pygopus, the method comprising:
- (a) testing a candidate compound and selecting the
15 compound for binding to an expressed product of a Pygopus gene;
- (b) testing the compound selected in (a) for its ability to inhibit Pygopus-mediated transcription activation of a Wnt-responsive gene; and optionally
- 20 (c) testing the compound selected in (b) in epithelial ovarian carcinoma or breast cancer cells for its ability to inhibit proliferation of the cells.
27. The method according to claim 26 wherein, in step (a), the candidate compound is tested and selected for
25 binding to a Pygopus protein.

28. The method according to claim 26 wherein, in step (a), the candidate compound is tested and selected for binding to a Pygopus mRNA.

29. The method according to any one of claims 26 to 28 wherein, in step (b), the candidate compound is tested for its ability to inhibit Pygopus-mediated transcription activation of Cyclin D1.

30. A method for obtaining an antisense polynucleotide which inhibits tumor cell proliferation, wherein the tumor cell express Pygopus, the method comprising:

(a) providing a polynucleotide which is antisense to a Pygopus gene, or antisense to a portion of a Pygopus gene;

(b) delivering the polynucleotide into epithelial ovarian carcinoma or breast cancer cells; and

(c) determining whether the delivered polynucleotide inhibits proliferation of the cancer cells.

31. A method for obtaining a compound which inhibits tumor cell proliferation, wherein the tumor cell express Pygopus, the method comprising:

(a) providing a short interfering RNA (siRNA) or siRNA-like molecule targeted to a Pygopus gene or to a portion of a Pygopus gene;

(b) delivering the siRNA or siRNA-like molecule into epithelial ovarian carcinoma or breast cancer cells; and

(c) determining whether the delivered siRNA or siRNA-like molecule inhibits proliferation of the cancer cells.

32. The method according to any one of claims 26 to 31 wherein the Pygopus gene is a human gene.

33. The method according to claim 32 wherein the Pygopus gene is hPygo2 (SEQ ID NO:1) or hPygo1 (SEQ ID
5 NO:3).

34. The method according to claim 30 or 31 wherein, in step (a), the portion of a Pygopus gene is the region from nucleotide 437 to 1156 of SEQ ID NO:1, or the region from nucleotide 253 to 1023 of SEQ ID NO:3.

10 35. A method for inhibiting tumor cell proliferation, the method comprising contacting the tumor cell with a proliferation-inhibiting amount of a compound which reduces Pygopus activity in the cell.

36. The method according to claim 35 wherein the tumor
15 cell is an epithelial ovarian carcinoma cell or breast cancer cell.

37. The method according to claim 35 or 36 wherein the compound reduces the ability of Pygopus to inhibit transcription activation of a Wnt-responsive gene.

20 38. The method according to claim 37 wherein the Wnt-responsive gene is Cyclin D1.

39. A method for inhibiting tumor cell proliferation, the method comprising delivering to the tumor cell a proliferation-inhibiting amount of a compound which reduces
25 expression of a Pygopus-encoding nucleic acid.

40. The method according to claim 39 wherein the tumor cell is an epithelial ovarian carcinoma cell or breast cancer cell.

41. The method according to claim 39 or 40 wherein the compound is a polynucleotide which is antisense to a Pygopus gene, or antisense to a portion of a Pygopus gene.

42. The method according to claim 39 or 40 wherein the
5 compound is a short interfering RNA (siRNA) or siRNA-like molecule targeted to a Pygopus gene or to a portion of a Pygopus gene.

43. The method according to any one of claims 39 to 42 wherein the Pygopus gene is a human gene.

10 44. The method according to claim 43 wherein the Pygopus gene is hPygo2 (SEQ ID NO:1) or hPygo1 (SEQ ID NO:3).

45. The method according to claim 41 or 42 wherein the
15 portion of a Pygopus gene is the region from nucleotide 437 to 1156 of SEQ ID NO:1, or the region from nucleotide 253 to 1023 of SEQ ID NO:3.

46. An antisense oligonucleotide targeted to hPygo2
(SEQ ID NO:1) in the region from nucleotide 437 to 1156 of
SEQ ID NO:1, wherein said antisense oligonucleotide
20 specifically hybridizes with said region and reduces the expression of hPygo2.

47. An antisense oligonucleotide targeted to hPygo1
(SEQ ID NO:3) in the region from nucleotide 253 to 1023 of
SEQ ID NO:3, wherein said antisense oligonucleotide
25 specifically hybridizes with said region and reduces the expression of hPygo1.

48. A short interfering RNA (siRNA) or siRNA-like
molecule targeted to hPygo2 (SEQ ID NO:1) in the region from

nucleotide 437 to 1156 of SEQ ID NO:1, wherein said siRNA or siRNA-like molecule reduces the expression of hPygo2.

49. A short interfering RNA (siRNA) or siRNA-like molecule targeted to hPygo1 (SEQ ID NO:3) in the region from
5 nucleotide 253 to 1023 of SEQ ID NO:3, wherein said siRNA or siRNA-like molecule reduces the expression of hPygo1.

50. The antisense oligonucleotide according to claim 46 having the sequence selected from the group consisting of SEQ ID NOS:5-14.

10 51. The antisense oligonucleotide according to claim 50 having the sequence of SEQ ID NO:9.

52. The siRNA or siRNA-like molecule according to claim 48 having the sequence selected from the group consisting of SEQ ID NOS:15-19.

15 53. The siRNA or siRNA-like molecule according to claim 52 having the sequence of SEQ ID NO:15 or 18.